

## REMARKS

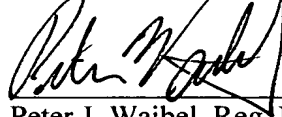
Entry of this preliminary amendment is respectfully requested.

This application is a divisional of copending application no. 09/420,347. Claims 3-6, 8-15, 17, 19-22, 25, 34, 35, 37-42 and 45-49 have been cancelled without prejudice or disclaimer. Claims 1, 2, 7, 16, 18, 23, 24, 26-33, 36, and 43-44 are amended to remove nonelected subject matter and to correct multiple dependencies. Claims 50-54 have been added. New claims 50-54 rewrite original claims 37, 41, and subject matter cancelled from pending claim 44. Claims 1, 2, 7, 16, 18, 23, 24, 26-33, 36, 43-44, and 50-54 are based on the corresponding claims as originally filed in the parent application and are directed to the subject matter of **Group VI** which has not elected in the parent application. No new matter is added.

Accordingly, claims 1, 2, 7, 16, 18, 23, 24, 26-33, 36, 43-44, and 50-54 are pending and at issue in this application.

It is believed that the claims are in condition for allowance, and a determination to that effect is earnestly solicited. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,



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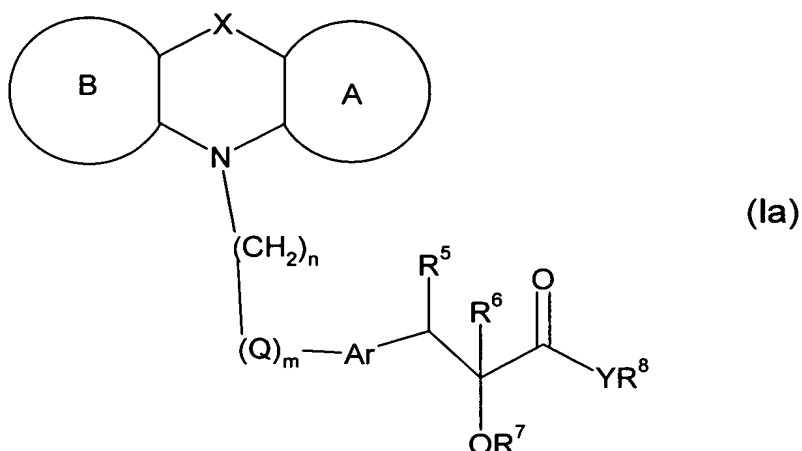


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PATENT TRADEMARK OFFICE

MARKED-UP VERSION OF THE CLAIMS SHOWING AMENDMENTS MADE

1. (Amended) A compound of formula (Ia)



wherein ring A<sub>1</sub> fused to the ring containing X and N<sub>1</sub> represents a 5-6 membered cyclic ring[,] optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro, cyano, formyl, or C<sub>1-12</sub>alkyl, C<sub>4-12</sub>-alkenynyl, C<sub>2-12</sub>-alkenyl, C<sub>2-12</sub>-alkynyl, C<sub>1-12</sub>alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC<sub>1-12</sub>alkyl, amino, acylamino, C<sub>1-12</sub>alkyl-amino, arylamino, aralkylamino, aminoC<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C<sub>1-12</sub>alkoxyC<sub>1-12</sub>alkyl, aryloxyC<sub>1-12</sub>alkyl, aralkoxyC<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkylthio, thioC<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR<sup>11</sup>, or -SO<sub>2</sub>R<sup>12</sup>, wherein R<sup>11</sup> and R<sup>12</sup> independently of each other are selected from hydroxy, halogen, perhalomethyl, C<sub>1-6</sub>alkoxy or amino optionally substituted with one or more C<sub>1-6</sub>alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

ring B<sub>1</sub> fused to the ring containing X and N<sub>1</sub> represents a 5-6 membered cyclic ring[,] optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro, cyano, formyl, or C<sub>1-12</sub>alkyl, C<sub>4-12</sub>-alkenynyl, C<sub>2-12</sub>-alkenyl, C<sub>2-12</sub>-alkynyl,

C<sub>1-12</sub>alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC<sub>1-12</sub>alkyl, amino, acylamino, C<sub>1-12</sub>alkyl-amino, arylamino, aralkylamino, aminoC<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C<sub>1-12</sub>alkoxyC<sub>1-12</sub>alkyl, aryloxyC<sub>1-12</sub>alkyl, aralkoxyC<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkylthio, thioC<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR<sup>11</sup>, or -SO<sub>2</sub>R<sup>12</sup>, wherein R<sup>11</sup> and R<sup>12</sup> independently of each other are selected from hydroxy, halogen, perhalomethyl, C<sub>1-6</sub>alkoxy or amino optionally substituted with one or more C<sub>1-6</sub>alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

X is [a valence bond, -(CHR<sup>9</sup>)-, -(CHR<sup>9</sup>)-CH<sub>2</sub>-, -CH=CH-, -O-, -O-(CHR<sup>9</sup>)-, -S-(CHR<sup>9</sup>)-, -(NR<sup>9</sup>)-CH<sub>2</sub>-, -(CHR<sup>9</sup>)-CH=CH-, -(CHR<sup>9</sup>)-CH<sub>2</sub>-CH<sub>2</sub>-, -(C=O)-,] -O-CH<sub>2</sub>-O-, [- (NR<sup>9</sup>)-,] -(NR<sup>9</sup>)-S(O<sub>2</sub>)-, [-CH=(CR<sup>9</sup>)-, -(CO)-(CHR<sup>9</sup>)-, -CH<sub>2</sub>-(SO)-, -S-, -(SO)-, -(SO<sub>2</sub>)-, -CH<sub>2</sub>-(SO<sub>2</sub>)-, -CH<sub>2</sub>-O-CH<sub>2</sub>-,] wherein R<sup>9</sup> is hydrogen, halogen, hydroxy, nitro, cyano, formyl, C<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, C<sub>1-12</sub>alkyl-amino, arylamino, aralkylamino, aminoC<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C<sub>1-12</sub>alkoxyC<sub>1-12</sub>alkyl, aryloxyC<sub>1-12</sub>alkyl, aralkoxyC<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkylthio, thioC<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR<sup>11</sup>, or -SO<sub>2</sub>R<sup>12</sup>, wherein R<sup>11</sup> and R<sup>12</sup> independently of each other are selected from hydroxy, halogen, C<sub>1-6</sub>alkoxy, amino optionally substituted with one or more C<sub>1-6</sub>alkyl, perhalomethyl or aryl;

Q is -O-, -S-, >SO<sub>2</sub>, >NR<sup>13</sup>, wherein R<sup>13</sup> is hydrogen or C<sub>1-6</sub>alkyl,

Ar represents arylene, heteroarylene, or a divalent heterocyclic group optionally substituted with one or more C<sub>1-6</sub>alkyl or aryl;

R<sup>5</sup> represents hydrogen, hydroxy, halogen, C<sub>1-12</sub>alkoxy, C<sub>1-12</sub>alkyl, C<sub>4-12</sub>-alkenynyl,

C<sub>2-12</sub>-alkenyl, C<sub>2-12</sub>-alkynyl or aralkyl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano; or R<sup>5</sup> forms a bond together with R<sup>6</sup>,

R<sup>6</sup> represents hydrogen, hydroxy, halogen, C<sub>1-12</sub>alkoxy, C<sub>1-12</sub>alkyl, C<sub>4-12</sub>-alkenynyl, C<sub>2-12</sub>-alkenyl, C<sub>2-12</sub>-alkynyl, acyl or aralkyl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano; or R<sup>6</sup> forms a bond together with R<sup>5</sup>,

R<sup>7</sup> represents hydrogen, C<sub>1-12</sub>alkyl, C<sub>4-12</sub>-alkenynyl, C<sub>2-12</sub>-alkenyl, C<sub>2-12</sub>-alkynyl, aryl, aralkyl, C<sub>1-12</sub>alkoxyC<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkoxycarbonyl, aryloxycarbonyl, C<sub>1-12</sub>alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl or heteroaralkyl groups[:], optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

R<sup>8</sup> represents hydrogen, C<sub>1-12</sub>alkyl, C<sub>4-12</sub>-alkenynyl, C<sub>2-12</sub>-alkenyl, C<sub>2-12</sub>-alkynyl, aryl, aralkyl, heterocyclyl, heteroaryl or heteroaralkyl groups; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

Y represents oxygen, sulphur or NR<sup>10</sup>, where R<sup>10</sup> represents hydrogen, C<sub>1-12</sub>alkyl, aryl, hydroxyC<sub>1-12</sub>alkyl or aralkyl groups or when Y is NR<sup>10</sup>, R<sup>8</sup> and R<sup>10</sup> may form a 5 or 6 membered nitrogen containing ring, optionally substituted with one or more C<sub>1-6</sub>alkyl;

n is an integer ranging from 1 to 4 and m is an integer ranging from 0 to 1[, provided that A or B does not represent phenyl];  
or a pharmaceutically acceptable salt thereof.

2. (Amended) [A] The compound according to claim 1, wherein ring A<sub>1</sub> fused to the ring containing X and N<sub>1</sub> represents a 5-6 membered cyclic ring[, optionally substituted with one or more hydrogen, halogen, perhalomethyl, hydroxy, cyano, or C<sub>1-7</sub>alkyl, C<sub>4-7</sub>-alkenynyl, C<sub>2-7</sub>-alkenyl, C<sub>2-7</sub>-alkynyl, C<sub>1-7</sub>alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC<sub>1-7</sub>alkyl, amino, acylamino, C<sub>1-7</sub>alkyl-amino, arylamino, aralkylamino, aminoC<sub>1-7</sub>alkyl, C<sub>1-7</sub>alkoxyC<sub>1-7</sub>alkyl, aryloxyC<sub>1-7</sub>alkyl, aralkoxyC<sub>1-7</sub>alkyl, C<sub>1-7</sub>alkylthio, thioC<sub>1-7</sub>alkyl, C<sub>1-7</sub>alkoxycarbonylamino,

aryloxycarbonylamino, aralkoxycarbonylamino, -COR<sup>11</sup>, or -SO<sub>2</sub>R<sup>12</sup>, wherein R<sup>11</sup> and R<sup>12</sup> independently of each other are selected from hydroxy, perhalomethyl or amino optionally substituted with one or more C<sub>1-6</sub>alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy or cyano.

7. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1, wherein ring B<sub>1</sub> fused to the ring containing X and N<sub>1</sub> represents a 5-6 membered cyclic ring[,] optionally substituted with one or more hydrogen, halogen, perhalomethyl, hydroxy, cyano, or C<sub>1-7</sub>alkyl, C<sub>4-7</sub>-alkenynyl, C<sub>2-7</sub>-alkenyl, C<sub>2-7</sub>-alkynyl, C<sub>1-7</sub>alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC<sub>1-7</sub>alkyl, amino, acylamino, C<sub>1-7</sub>alkyl-amino, arylamino, aralkylamino, aminoC<sub>1-7</sub>alkyl, C<sub>1-7</sub>alkoxyC<sub>1-7</sub>alkyl, aryloxyC<sub>1-7</sub>alkyl, aralkoxyC<sub>1-7</sub>alkyl, C<sub>1-7</sub>alkylthio, thioC<sub>1-7</sub>alkyl, C<sub>1-7</sub>alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR<sup>11</sup>, or -SO<sub>2</sub>R<sup>12</sup>, wherein R<sup>11</sup> and R<sup>12</sup> independently of each other are selected from hydroxy, perhalomethyl or amino optionally substituted with one or more C<sub>1-6</sub>alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy or cyano.

16. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Q is -O- or -S-.

18. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Ar represents arylene, heteroarylene, or a divalent heterocyclic group optionally substituted with one or more C<sub>1-6</sub>alkyl or aryl;  
R<sup>5</sup> represents hydrogen, hydroxy, halogen, C<sub>1-7</sub>alkoxy, C<sub>1-7</sub>alkyl, C<sub>4-7</sub>-alkenynyl, C<sub>2-7</sub>-alkenyl, C<sub>2-7</sub>-alkynyl; or R<sup>5</sup> forms a bond together with R<sup>6</sup>,  
R<sup>6</sup> represents hydrogen, hydroxy, halogen, C<sub>1-7</sub>alkoxy, C<sub>1-7</sub>alkyl, C<sub>4-7</sub>-alkenynyl, C<sub>2-7</sub>-alkenyl, C<sub>2-7</sub>-alkynyl; or R<sup>6</sup> forms a bond together with R<sup>5</sup>,  
R<sup>7</sup> represents hydrogen, C<sub>1-7</sub>alkyl, C<sub>4-7</sub>-alkenynyl, C<sub>2-7</sub>-alkenyl, C<sub>2-7</sub>-alkynyl, aryl, aralkyl, C<sub>1-7</sub>alkoxyC<sub>1-7</sub>alkyl, C<sub>1-7</sub>alkoxycarbonyl, aryloxycarbonyl, C<sub>1-7</sub>alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl or heteroaralkyl groups;

R<sup>8</sup> represents hydrogen, C<sub>1-7</sub>alkyl, C<sub>4-7</sub>-alkenynyl, C<sub>2-7</sub>-alkenyl, C<sub>2-7</sub>-alkynyl, aryl, aralkyl, heterocyclyl, heteroaryl or heteroaralkyl;

Y represents oxygen, sulphur or NR<sup>10</sup>, where R<sup>10</sup> represents hydrogen, C<sub>1-7</sub>alkyl, hydroxyC<sub>1-7</sub>alkyl;

n is an integer ranging from 2 to 3 and m is an integer ranging from 0 to 1.

23. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein A is 5 membered cyclic ring containing S.

24. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein B is 5 membered cyclic ring containing S.

26. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein n is 2.

27. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Q is -O-.

28. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein m is 1.

29. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Ar is phenylene.

[In another preferred embodiment, the present invention is concerned with compounds of formula I wherein R<sup>5</sup> is H.]

30. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein R<sup>6</sup> is H.

31. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein R<sup>7</sup> is ethyl.

32. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Y is oxygen.

33. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein R<sup>8</sup> is H.

36. (Amended) A pharmaceutical composition comprising[, ] as an active ingredient, [a] the compound according to [any one of the preceding compound claims] claim 1 or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier or diluent.

43. (Amended) A method for the treatment [and/or prevention] of conditions mediated by nuclear receptors, in particular the Peroxisome Proliferator-Activated Receptors (PPAR), the method comprising administering to a subject in need thereof an effective amount of [a] the compound according to [any one of the preceding compound claims] claim 1 or a pharmaceutically acceptable salt thereof[, or of a composition according to anyone of the preceding claims 36-41].

44. (Amended) A method for the treatment [and/or prevention] of diabetes [and/or obesity], the method comprising administering to a subject in need thereof an effective amount of [a] the compound according to [anyone of the preceding compound claims] claim 1 or a pharmaceutically acceptable salt thereof[, or of a composition according to anyone of the preceding claims 36-41].